Synthesis, Characterization Of Various Coumarin Derivatives

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Received 20 / 09 / 2011
Accepted 08 / 12 / 2011

الخلاصة

في هذه الدراسة تم تحضير 3-اسيتايل الكومارين (1) من مفاعلة السالسيلديهايد مع اسيتواسيتات الاثيل بوجود الببريدين. ثم مفاعلة الناتج (1)مع البروم بوجود الكلوروفورم لينتج 3-(2-برومو اسيتايل كومارين)(2). مركب (3) يحضر بمفاعلة المركب (2) مع الايميدازول لينتج المركب (3) الذي نفاعله مع الهيدرازين هيدريت والفنيل هيدرازين و2-4-ثنائي نايترو فنيل هيدرازين لينتج المركبات (4و5و6) على التوالي. ثم مفاعلة المركب(3) مع مختلف الامينات الاروماتية والاليفاتية لينتج المركبات (7-15). شخصت المركبات الناتجة بواسطة الطرائق الفيزياوية والتحليلات الطيفية المتوفرة (IR,U.V).

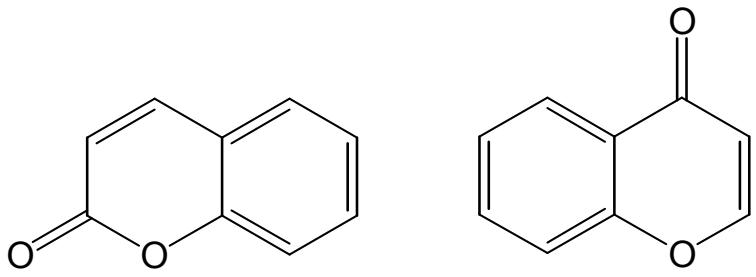
Abstract

3-acetyl coumarin (1) was prepared by reacting salicyldehyde with ethylacetoacetate.3-(2-bromoacetyl coumarin (2) was also prepared by reacting 3-acetyl coumarin with bromine in chloroform solution. Reaction of compound (2) with imidazol in dioxan solution to gave 3-(1H-imidazol-1yl-acetyl) coumarin(3). Compounds (4,5,6) were synthesized by the reaction of compound (3) with hydrazine hydrate, phenyl hydrazine, 2,4-dinitro-phenylhydrazine respectively. Compound (7-15) were synthesized by the reaction of compound (3) with various aromatic and aliphatic amines. The structures of all the synthesized compounds have been established on the basis of physical, spectral (IR, U.V) data.

Key words: different coumarin, derived imidazole, schiffbase,phenyl hydrazine coumarin.

Introduction

Coumarins owe their class name to 'Coumarou', the vernacular name of the tonka bean (*Dipteryx odorata* Willd., Fabaceae), from which coumarin itself was isolated in 1820[1]. Coumarin is classified as a member of the benzopyrone family of compounds, all of which consist of a benzene ring joined to a pyrone ring [2]. The benzopyrones can be subdivided into the benzo-a-pyrones to which the coumarins belong and the benzo-g-pyrones, of which the flavonoids are principal members (Fig. **1.1**).



[A] a-Benzopyrone **[B] g-Benzopyrone**

Fig. (1.1): The chemical structures of benzopyrone subclasses, with the basic coumarin structure (benzo-a-pyrone) [A], and flavonoid (benzo-g-pyrone) structure [B].

There are four main coumarin sub-types: the simple coumarins, furanocoumarins, pyranocoumarins and the pyrone-substituted coumarins (The simple coumarins (e.g. coumarin, 7-hydroxycoumarin and 6,7-dihydroxycoumarin), are the hydroxylated, alkoxylated and alkylated derivatives of the parent compound, coumarin, along with their glycosides. Furanocoumarins consist of a five-membered furan ring attached to the coumarin nucleus, divided into linear or angular types with substituents at one or both of the remaining benzoid positions. Pyranocoumarin members are analogous to the furanocoumarins, but contain a six-membered ring. Coumarins substituted in the pyrone ring include 4-hydroxycoumarin [3]. The synthetic compound, warfarin, belongs to this coumarin subtype. By virtue of its structural simplicity coumarin has been assigned as head of the benzo-a-pyrones, although it is generally accepted that 7-hydroxycoumarin be regarded as the parent compound of the more complex coumarins Genistein is an isoflavone and belongs to the benzo-g- pyrones. It is a natural component of soy and has been intensively investigated as a chemopreventitive agent,mainly against hormonally regulated breast and

prostate cancers in animal models [5]. Coumarins comprise a very large class of compounds found throughout the plant kingdom [6-8]. They are found at high levels in some essential oils, particularly cinnamon bark oil (7,000 ppm), cassia leaf oil (up to 87,300 ppm) and lavender oil. Coumarin is also found in fruits (e.g. bilberry, cloudberry), green tea and other foods such as chicory [9]. Most coumarins occur in higher plants, with the richest sources being the Rutaceae and Umbelliferae. Although distributed throughout all parts of the plant, the coumarins occur at the highest levels in the fruits, followed by the roots, stems and leaves. Environmental conditions and seasonal changes can influence the occurrence in diverse parts of the plant [3]. Recently six new minor coumarins have been isolated from the fruits and the stem bark of *Calophyllum dispar* (Clusiaceae). The genus *Calophyllum*, which comprises 200 species, is widely distributed in the tropical rain forest where several species are used in folk medicine [10]. Although most of the natural coumarins in existence have been isolated from the higher plants, some members have been discovered in microorganisms Some important coumarin members have been isolated from microbial sources e.g. novobiocin and coumermycin from *Streptomyces*, and aflatoxins from *Aspergillus* species [11, 12]. The aflatoxins are a group of highly toxic fungal metabolites and the most commonly occurring member of the group is aflatoxin B1 [3].

Experimental

Chemicals and instrumentation

All chemicals were purchased from Flucka and BDH chemical Ltd. The melting points were measured on an electrothermal 9300 engineering Ltd and were uncorrected. IR spectra were recorded on infrared spectrophotometer Model Tensor 27, Bruker Co.,Germany,using KBr discs.UV spectra were recorded on Shimadzu double-beam spectrophotometer UV -210 A using chloroform as a solvent. The theoretical calculations were computed using semi-empirical AM1 module in the CS chem office molecular modeling package.the data obtained from the minimized geometry were used for the theoretical calculations.

Synthesis of 3-acetyl -2H-chromen-2-one[13] (1)

To a cold mixture of salicylaldehyde (12.2g,0.10mole) and ethylacetoacetate (13g ,0.10 mole) was added 1 g of piperidine With continuous shaking. The solid separated was washed with ethanol. Crystallization of the solid from water gave yellow needle crystals.m.p (121-122˚C) Lit (122˚C) pure 3-acetyl coumarin.

Synthesis of 3-(*2*-bromoacetyl) -2H-chromen-2-one [14] (2)

A solution of bromine (4 g,13ml) in chloroform was added by shaking to a solution of 3-acetylcoumarin (4.7g, 0.025 mole) in chloroform. The mixture was heated under reflux for 1 h and cooled. The solid separated was washed with ether and crystallized from ethanol-chloroform (2:1) gave yellow needle crystals m.p(167-168˚C) let(164-168 ˚C).

Preparation of 3- (1H-imidazol-1yl-acetyl) -chromen-2-one [15] (3)

A mixture of 3- (bromo acetyl))-2H-chromen-2-one (2.65g,0.01mole) and imidazole (2.54g, 0.01mole) in 1,4 dioxan (30 mL) was stirred for 2 hrs on magnetic stirrer. The precipitate obtained was filtered, washed thoroughly with acetone and the crude product was recrystallized from ethanol to gave yellow crystalline powder m.p(196-198˚C).

Preparation of 3-[(1Z)-2-(1H-imidazol-1-yl)-1-(2- phenyl hydrazinylidene)ethyl] - chromen-2-one, [16] (4)

A mixture of (1H-imidazol-1yl-acetyl)) -2H-chromen-2-one (3)(0.5 gm, 0.002 mole), phenyl hydrazine (0.43g, 0.004 mole) and sodium acetate (0.3g, 0.004 mole) in10-15mL of ethanol was refluxed for 2 hrs then cooled. The reaction mixture was poured into ice cold water and the yellow precipitate obtained was filtered and recrystallized from ethanol gave light yellow powder m.p(142-144˚C).

Preparation of 3-[(1Z)-2-(1H-imidazol-1-yl)-1-(2- drazinylidene)ethyl] – chromen-2-one, [16] (5)

A mixture of (1H-imidazol-yl-acetyl) coumarin (3) (0.5 gm, 0.002 mole), hydrazine hydrate (0.2 g. 0.004 mole) and sodium acetate (0.3g, 0.004 mole) in10-15mL of ethanol was refluxed for 2 hrs then cooled. The final reaction mixture was poured into an ice cold water and the yellow precipitate obtained was filtered and recrystallized from ethanol to give light yellow crystals m.p(148-150˚C).

3-{1-[(2,4-Dinitro-phenyl)-hydrazono]-2-imidazol-1-yl-ethyl}-chromen-2-one[16](6)

A mixture of (1H-imidazol-yl-acetyl) coumarin (3) (0.5 gm, 0.002 mole), 2,4-dinitrophenyl hydrazine (0.79g, 0.004 mole) and sodium acetate (0.3g, 0.004 mole) in10-15mL of ethanol was refluxed for 2 hrs, cooled. The reaction mixture was poured into an ice cold water and the yellow precipitate obtained was filtered and recrystallized from ethanol to give slight yellow crystals m.p(260-262˚C).

Preparation of imines derived from(1H-imidazol-yl-acetyl)coumarin[17] (7-15)

A mixture of (1H-imidazol-yl-acetyl) coumarin (3)(1,27g, 0.005mole) and different aromatic amines (0.005mole) in (20 ml) absolute ethanol and add one Drop glacial acetic acid then reflux for 3 hours. concentrate the

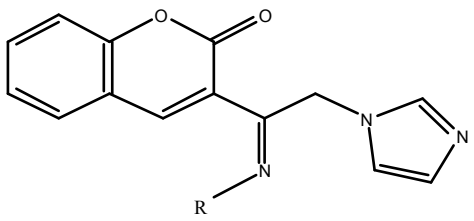
solution for half then cold and The solid separated was washed with water and crystallized from ethanol gave compounds (7-15)

Table(1): some physical properties for compounds (1-3)

Comp. No	structure	color	m.p °C	Yield %	m.p °C lit
1	3-acetyl coumarin	Needle crystal yellow	121-122	70	122[13]
2	3-(2-bromoacetyl)coumarin	Needle crystal yellow	167-168	38	163-165[14]
3	3-(1 H-imidazol-yl-acetyl)coumarin	Crystalline yellow powder	196-198	65	

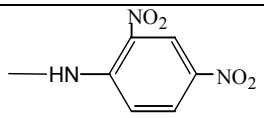
Table(2): Some spectral data for compounds(1-3)

Comp.No	IR(KBr),ν (cm^{-1})				U.V($CHCl_3$) λmax(nm)
	C=0 lactone	C=O acetyl	C=N	C=C	
1	1735	1700		1635	309
2	1740	1690		1630	304
3	1724	1693	1604	1633	312



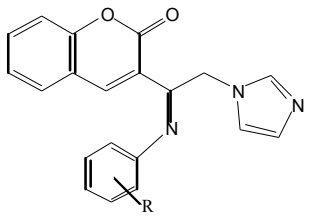
Compounds(4,5,6)

Table (3): some physical properties for compounds (4-6)

Comp .No	R	m.p °C	Yield%
4	-NH_2	148-150	70
5	-NH-ph	142-144	72
6		260	65

Table(4): Some spectral data for compounds (4-6)

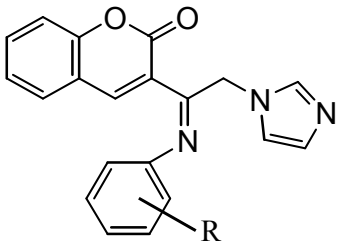
Comp. NO.	IR(KBr), ν (cm^{-1})			U.V($CHCl_3$) λmax(nm)
	C=O lactone	C=N	N-H	
4	1710	1605	3232	301
5	1708	1600	3238	292
6	1711	1602	3225	310



Compounds(7-15)

Table(5): some physical properties for compounds (7-15)

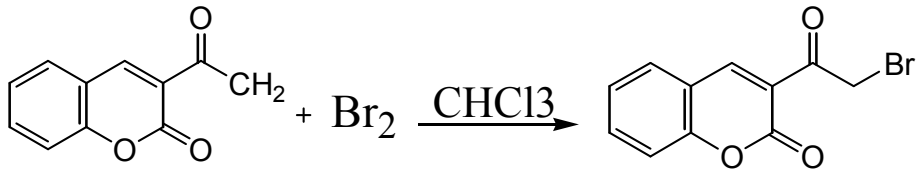
Comp. No.	R	m.p ˚C	Yield%
7	H	102	60
8	2-COOH	110	62
9	4-OH	106	70
10	2-NH_2 4-CH_3	163	60
11	2-OH	160	55
12	3-OH	173	62
13	CH_2CH_3	142	82
14	2-Cl	120	52
15	2-NO_2	115	66



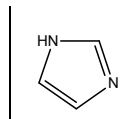
Compounds(7-15)

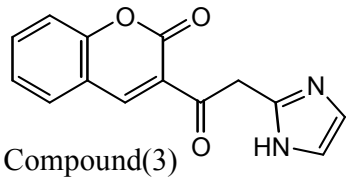
Table(6):Some spectral data for compounds(7-15)

Comp. No.	R	IR(KBr), ν(cm^{-1})			U.V($CHCl_3$) λmax(nm)
		C=O lactone	C=N	NH	
7	H	1708	1600	3325	305
8	2-COOH	1720	1600	3320	302
9	4-OH	1732	1602	3340	314
10	2-NH_2 4-CH_3	1719	1610	3370	325
11	2-OH	1710	1595	3355	302
12	3-OH	1725	1999	3365	309
13	CH_2CH_3	1730	1610	3344	312
14	2-Cl	1715	1602	3360	320
15	2-NO_2	1717	1604	3365	333

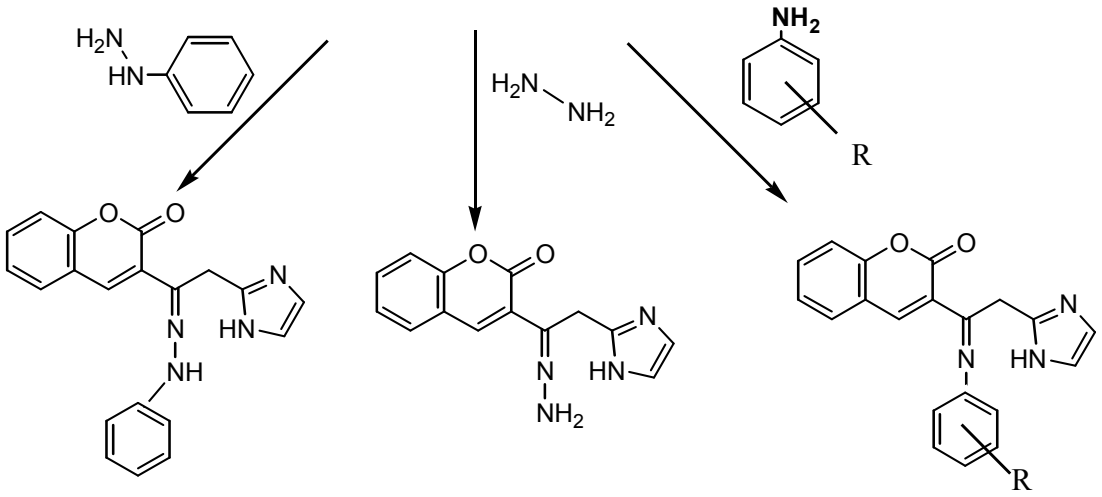


Compound(1) Compound(2)



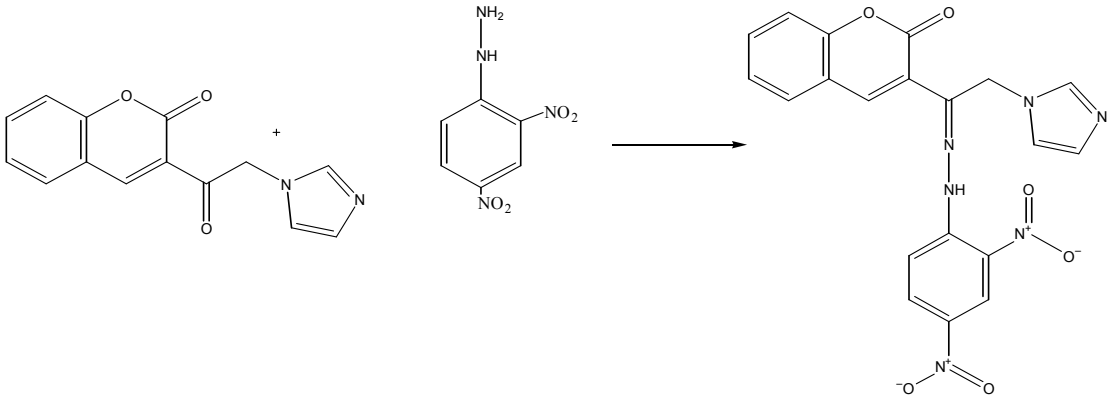


Compound(3)



compound(5) compound(4) compound(7-15)

R=H,2COOH,4-OH,2NO_2CH_3,2-OH,3-OH,CH_2CH_3,2-Cl,2-NO_2



Compound(6)

RESULTS AND DISCUSSION

In this study,3-acetyl coumarin and 3-(2-bromoacetyl)coumarin were prepared by section(1,2).3-(1H-imidaol-1yl-acetyl) coumarin (compound(3). compound(3) was elucidated by U.V and infrared spectra(table 2). the I.R spectrum of compound(3) showed C=O str. Of lactone at 1724 cm^{-1}, C=N str. Of imidaol at 1604cm^{-1} This compound was treated with hydrain hydrate, phenyl hydrazine,2,4-dinitrophenyl-hydrazin to give the compounds s hydrazon derivatives. The I.R spectrum of 4,5,6 compounds showed C=O str. Of lactone at (1708-1712) cm^{-1} because the conjugated between the double bond in the imine and the double bond in the coumarin, N-H str at 3223 cm^{-1} C=N str. At (1600-1605) cm^{-1} and disappearance of band at 1693 cm^{-1} indicated the formation of the compounds the compound (3) was treated with different Aromatic and aliphatic amines to form imines. the I.R spectrum of (7-15) showed C=O str. Of lactone approximatly at (1708-1711) cm^{-1}, C=N str.(1595-1610) cm^{-1} N-H str. (3320-3365). the U.V spectra of compound(3)show λmax at 312 nm The U.V spectra of compounds(4-6) showed high λmax at 310 nm due to conjugated between double bond and CN and the U.V spectra of compounds (7-15) showed high λmax 333 nm due to conjugated between double bond and CN.

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